UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: September 21, 2021

SUBJECT: Efficacy Review for ERCOPURE BCD-7.5,
EPA Reg. No. 9150-8
Action Code Case No: 00218032
E-submission No. 53740

FROM: Cesar E. Cordero
Efficacy Branch
Antimicrobials Division (7510P)
Date Signed: September 17, 2021

THRU: Sophie Nguyen
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Date Signed: September 21, 2021

TO: Demson Fuller, PM 32/Wanda Henson
Regulatory Management Branch I
Antimicrobials Division (7510P)

APPLICANT: International Dioxcide Inc.

Formulation from the Label:

Active Ingredient(s)	% by wt.
Sodium Chlorite	7.5%
Other Ingredients	92.5%
Total	100.0%

I. BACKGROUND

Product Description (as packaged, as applied): Concentrated Liquid (Dilutable)

Submission type: Label Amendment

Currently registered efficacy claim(s): Potable water and wastewater disinfection, microbial control in food processing plants, dairies, bottling plants and breweries, food plants process, poultry processing water. In food processing facilities as a terminal food contact surface sanitizing rinse. To control bacteria in irrigation and irrigation water systems (to control bacteria, algae, and slime), aqueous disinfection systems for CIP cleaning. Industrial process water treatment (oilfield injection water, white water paper mill systems and recirculating cooling towers: control of microbial slime.

Requested action(s): Amend the label to add claims for reduction of suspended *Legionella pneumophila* in "secondary treatment of potable water systems"

Documents considered in this review:

- Cover letter from applicant to EPA dated 8/13/2020
- Proposed label dated 8/13/2020
- Data Matrix (EPA Form 8570-35) dated 8/13/2020
- 1 efficacy studies and 1 document titled "Discussion of Secondary Potable Water Treatment Efficacy Study) (MRIDs 51186501 and 51186502 respectively)
- Confidential Statement of Formula (EPA Form 8670-4) dated 11/29/2006 (Accessed from Documentum).
- Protocol: Standard Operating Procedure for Measuring Antimicrobial Efficacy in Secondary Potable Water Treatment (MRID 49741801 (2015))
- Protocol Review for 1706PA4 (DP Barcode: D430459)

II. AGENCY STANDARDS FOR PROPOSED CLAIMS

1. There are no agency standards for the proposed claims.

III. PROPOSED DIRECTIONS FOR USE

"[[†] **[SECONDARY TREATMENT OF POTABLE WATER SYSTEMS:** For secondary treatment of potable water systems a chlorine dioxide residual concentration of 0.20 – 0.75 ppm must be monitored and maintained through the system for antimicrobial treatment and suspended Legionella pneumophila reduction. Monitor the system to ensure that chlorite concentration does not exceed its maximum contaminant level (MCL) of 1 ppm and that chlorine dioxide does not exceed its maximum residual disinfection level (MRDL) of 0.8 ppm. Residual chemistry and byproducts must be monitored as required by the National Primary Drinking Water Regulations (40 CFR Part 141), EPA Safe Drinking Water Act, and state drinking water standards.

Chlorine dioxide can serve as an important part of the program for the reduction of Legionella bacteria in potable water systems. A residual concentration of 0.09 ppm chlorine dioxide has been shown in laboratory testing to reduce Legionella pneumophila ATCC 33152 bacteria within 5 minutes following initial dose. The use of this product is one component of a Legionella risk reduction strategy that may be included as part of an overall strategy for managing Legionella risk in building water systems, which is recommended by the American Society of Heating,

Refrigerating and Air-Conditioning Engineers (ASHRAE) Standard 188-2015, a practice standard that establishes minimum legionellosis risk management requirements for building water systems. Under actual operating conditions, chemical treatment alone may not be an effective approach for Legionella control, risk mitigation from LDB or for the prevention of Legionnaires' disease."

Use of this product in public water systems (drinking water utilities) triggers monitoring and compliance requirements under 40 CFR 141. Among other requirements the user of this product is required to conduct daily monitoring for chlorine dioxide and chlorite at the point of addition and to comply with standards for chlorine dioxide and chlorite. The user of this product is required to contact State or primary drinking water programs to determine specific monitoring, compliance, reporting, and record-keeping requirements in order to avoid adverse human health effects and/or non-compliance with such requirements.]

IV. STUDY SUMMARIES

1.	**MRID**	51186501		
Study Objective		To evaluate the efficacy of secondary potable water treatment chemical methods against bacteria.		
Testing Lab; Lab Study ID		ALG; A28880		
Experimental Start Date		12/03/2019	**Study Completion Date:**	04/27/2020
Test organism(s) **☒ 1 ☐ 2 ☐ 3 ☐ 4+**		*Legionella pneumophila* (ATCC 33152)		
Test Method		810.2300; Protocol No. INT01052019.CUST		
Application Method		Dilutable solid (tablet)		
Test Substance Preparation	**Name/ID**	Adox (TM) BCD-7.5 (Adox is the previous brand name for ERCOPURE™ BCD-7.5 / Reg. No. 9150-8)		
	Lots **☐ 1 ☐ 2 ☒ 3**	1803222AHE, 1902181AHA and 1903071AHA		
	Preparation	Tested concentration: Nominal Tested Dilution: Diluted to ~0.8 ppm chlorine dioxide (Range between 0.09 - 0.84 ppm). Individual concentrations captured in Reviewer comments below. Diluent: Sterilized tap water		
Soil load		N/A		
Carrier type, # per lot		Tested against suspended *Legionella pneumophila*; test water was standard tap water from a city water faucet, which was autoclaved sterilized at 121°C		
Test conditions		Contact time: 5 min, 15 min and 30 min Temperature: 20±2°C Relative humidity: N/A		
Neutralizer		Letheen Broth+ 0.07% Lecithin+ 0.5% Tween 80		
Reviewer comments (i.e. protocol deviations and amendments, retesting, control failures, etc.)		No protocol amendments or deviations reported.		

Test Substance	Amount of Stock Solution Added	Timepoint (minutes)	Preparations Out of Range	Colorimeter Readout Per Test Flask (ppm)
1902181AHA	8.23 mL	0	1.04 ppm*	0.72, 0.84
		5	Not Applicable	0.09, 0.60
		15		0.53, 0.50
		30		0.56, 0.80
1903071AHA	9.35 mL	0	0.92 ppm**	0.84, 0.83
		5	Not Applicable	0.52, 0.60
		15		0.61, 0.75
		30		0.73, 0.50
1803222AHE	6.81 mL	0	Not Applicable	0.76, 0.70
		5		0.43, 0.44
		15		0.33, 0.36
		30		0.33, 0.64

Timepoints other than Time Zero contained the test organism and these flasks were swirled at the start of testing.
*Further diluted with 105.0 mL sterile tap water and measured again for use in testing.
**Further diluted with 30 mL sterile tap water and measured again for use in testing.

V. STUDY RESULTS

Reduction of suspended *Legionella* in secondary water treatment

Results					Carrier Population CFU/mL (Avg. Log_{10})
Batch #	**Replicate #**	**Residual chlorine dioxide reading***	**Geometric Mean (Mean Log_{10} Density)**	**Log_{10} Reduction**	
5-minute contact time					
1902181AHA	**1**	0.09 ppm	<1.00 (<0.00 Log_{10})	>7.15	1.16×10^7 (7.07)
	2	0.60 ppm			
1903071AHA	**1**	0.52 ppm	<1.00 (<0.00 Log_{10})	>7.15	
	2	0.60 ppm			
1803222AHE	**1**	0.43 ppm	<1.00 (<0.00 Log_{10})	>7.15	
	2	0.44 ppm			
15-minute contact time					
1902181AHA	**1**	0.53 ppm	<1.00 (<0.00 Log_{10})	>7.15	1.03×10^7 (7.01)
	2	0.50 ppm			
1903071AHA	**1**	0.61 ppm	<1.00 (<0.00 Log_{10})	>7.15	
	2	0.75 ppm			
1803222AHE	**1**	0.33 ppm	<1.00 (<0.00 Log_{10})	>7.15	
	2	0.36 ppm			
30-minute contact time					
1902181AHA	**1**	0.56 ppm	<1.00 (<0.00 Log_{10})	>7.15	2.69×10^7 (7.36)
	2	0.80 ppm			
1903071AHA	**1**	0.73 ppm	<1.00 (<0.00 Log_{10})	>7.15	
	2	0.50 ppm			
1803222AHE	**1**	0.33 ppm	<1.00 (<0.00 Log_{10})	>7.15	
	2	0.64 ppm			

***Measured using a Lovibond MD100 colorimeter.**

VI. STUDY CONCLUSIONS

MRID	Claim	Surface Type	Application Method(s) and Dilution*	Contact Time	Soil load	Diluent	Organism(s)	Data support tested conditions?
51186501	Reduces suspended *Legionella pneumophila* in "secondary treatment of potable water systems"	Standard tap water from a city water faucet, sterilized at 121°C (to represent secondary water systems)	Dilutable liquid	5, 10 and 30 minutes	None	Autoclave sterilized tap water	• *Legionella pneumophila (ATCC 33152)*	**No, see comments in section VII below**

* A stock solution of chlorine dioxide was generated for each test batch using the prepared tap water. A 0.200 ml aliquot of ADOX BCD-7.5 (~7.5% sodium chlorite) was added into a 100 ml bottle, per batch. A 5.0 ml aliquot of 10% HCI solution was then pipetted into the bottle and gently swirled for a few seconds. A stopwatch was started, and the bottle was covered with parafilm. After 2 minutes, the parafilm was removed from the bottle and 95.0 ml of prepared sterile tap water was poured into the bottle. The bottle was capped and then slowly inverted 4 times to mix. The tap water demand was ~150 µL stock solution per 200 ml tap water.

VII. LABEL COMMENTS

Label Date/ID: 20200813

1. The proposed label claims that the product, **ERCOPURE™ BCD-7.5**, applied at a chlorine dioxide residual concentration of 0.20 – 0.75 ppm in sterile tap water, is an effective treatment for reducing the levels of suspended *Legionella pneumophila* (ATCC 33152) when used as a secondary treatment of potable water systems with no soil load indicated within 5-minutes contact time (not to exceed 30 min):

   These claims are **not acceptable** as they are not supported by the submitted data. The agency does not currently have standards for the requested claim. We strongly recommend that the registrant considers submitting a protocol for agency review that is tailored to the product and the intended use and application before generating and submitting efficacy data. At this time, please remove all references to *Legionella pneumophila* reduction claims.

   The list of deficiencies is as follows:

   1. Registrant submitted this amendment request and referenced a previously approved claim for the "substantially similar" product, EPA. Reg. No. 1706-244. Note, the previously approved protocol is product-specific and was reviewed based on the best available resources at the time of approval. However, the team has since consulted with internal and external experts regarding the complexity of potable water systems and *Legionella* testing. Additionally, the agency is currently considering guidance that could impact claims for planktonic *Legionella* reduction. Therefore, based on the current knowledge, this testing approach is not sufficient to support new *Legionella* reduction claims for secondary potable water treatment.
      a. The referenced product, HYG-25, has more than 3 times the active concentration than that of ERCOPURE BCD-7.5%. It is unclear how the low concentration of sodium chlorite in ERCOPURE BCD-7.5% would affect the amount of chlorine generated in the water and how the monitoring and management process would be conducted to maintain the efficacious concentration in the water.
      b. The characteristics of water used in testing were not representative of those in potable water systems
         - No soil load reported for efficacy testing. Total Dissolved Solids (TDS) in drinking water in the U.S. can range between 50 – 1000 ppm. EPA establishes a Secondary National Drinking Water Standard for TDS of 500 ppm.
         - Only one test water was utilized that represented idyllic conditions. Secondary potable water systems can come in different ranges of TDS, chemistry, temperature, etc. Drinking water quality parameters (e.g., TDS, water treatment, pH, temperature, etc.) can vary between locations and/or over time, which could potentially impact the dosing and/or effectiveness of the product. These variables were not accounted for in the protocol.
         - The autoclaving process of the test water may have inhibited certain interferents that would be present in potable water systems. The data were also generated with an acidified solution.

It is unclear how this represents the water intended to be treated in a potable water system. The test water does not represent the worst-case scenario.

- The method mentions that ClO_2 was minimally measured following each exposure period. It is unclear what this means in terms of the consistency in the level of ClO_2 in the test water and its effect on efficacy throughout testing. How does this ensure that ClO_2 is continuously maintained in the potable water systems?

c. On labeling:
    - Methods to continuously manage and monitor the residual chlorine is unclear from the label.
    - It is unclear what the dosing frequency is or where the dosing locations would be to continuously generate the efficacious concentration.
        - At what locations in the water system will be considered treated (bulk storage, point of use)?
        - Considering the recirculation loop, how does the product address/reconcile elevated chlorine/acidified treated water with non-elevated chlorine/acidified water?
        - How is this managed if there are multiple service connections?
        - The label (page 4) references the initial dose after 5 minutes. Would there be follow-up doses?
        - For the initial dose in the system, it is not clear from the label when the water in a system is treated as a function of distance to the point of use, the number of branches in the water system, water system malfunctions, variable degrees of pressurization, etc.
    - What is the impact of heating from heating element on treated water and prior to treating the water (i.e., if the water heater reserves are to be treated)?
    - The label/method lacks clear instructions for aged water systems with the challenges of water stagnation, poor recirculation, inadequate routine flushing to include dead legs, etc.